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CISTERNOGRAMS IN THE PRIMATE
MACACA MULATTA

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ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE
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FOREWORD
(Nontechnical summary)

The cerebrospinal fluid (CSF) fills the ventricles within the brain (where it is produced) and bathes the surface of the brain. Its flow from the site of production to the region where it is absorbed can be imaged with a scintillation camera by injecting human serum albumin tagged with a radioisotope of moderately low energy and relatively short physical and biological half-life (technetium-99m) into the CSF space at the cisterna magna. This process is called cisternography.

In this report, the normal cisternographic patterns observed in the rhesus monkey (Macaca mulatta) are presented. The radiopharmaceutical migrates with the CSF flow from the cisterna magna (where it is injected) around the brainstem and surfaces of the brain toward the midline region (where it will be absorbed) within 4 hours. Radioisotope does not normally enter the ventricles within the brain. The CSF spaces visualized on the cisternograms were correlated with the anatomy of the basilar cisterns (through which the CSF flows) by casting these basilar cisterns with latex.

Cisternograms from monkeys with experimental communicating hydrocephalus are presented for comparison with the normal series. These animals have a pathological defect in the CSF flow and absorption pattern which is reflected in cisternographic studies. Radiopharmaceutical does not migrate over the brain surfaces in these animals, but enters the ventricles within the brain. Cisternography has proven to be a useful technique for demonstrating these alterations in CSF flow. The similarity of the patterns observed in these animals with those seen in patients with communicating hydrocephalus adds to the validity of the nonhuman primate model for further study of this disease.

ABSTRACT

Normal imaging of cerebrospinal fluid (CSF) flow in the primate Macaca mulatta using ^{99m}Tc labeled human serum albumin shows flow from the basal cisterns over the cerebral cortex in 4 hours. Anatomical correlation of basal cisterns with cisternographic images was demonstrated with latex casts of the normal CSF spaces. Cisternographic images from nonhuman primates with experimental communicating hydrocephalus have entry of radiopharmaceutical into the lateral ventricles and are presented for comparison. Cisternography is a useful technique for evaluating such primate disease models, since normal and pathologic images parallel those obtained in man.

I. INTRODUCTION

Cisternography or the imaging of the flow of cerebrospinal fluid (CSF) by the use of radiopharmaceuticals is currently assuming an important role in diagnostic neurology. This relatively safe, atraumatic, and reliable method can provide both anatomical and physiological data concerning abnormalities of CSF spaces and of CSF dynamics. Cisternography has been utilized most frequently in the diagnosis of communicating hydrocephalus, both in its detection² and in the selection of patients for CSF diversionary shunt therapy.⁶

Animal models have been developed recently to study the production, movement, and absorption of CSF in both noncommunicating and communicating hydrocephalus.^{1,3-5,7,9} Therefore, it is necessary to establish normal measurements and image patterns, and to define the anatomical structures and CSF spaces visualized in radionuclide scans. Normal radioisotope cisternograms of the dog have been presented elsewhere^{8,10} and although one of us (AEJ, Jr.) has performed over 200 canine cisternograms, this animal is less than ideal for the acquisition of data to relate to humans.

The purpose of this study is to present the normal cisternographic patterns seen in the nonhuman primate, specifically Macaca mulatta, to correlate the structures visualized with anatomical data, and to compare normal cisternographic patterns with those seen in experimental communicating hydrocephalus in the same species.

II. MATERIALS AND METHODS

Cisternograms. Rhesus monkeys weighing 3 to 4 kilograms were anesthetized with intravenous sodium pentobarbital. The back of the neck was shaved and prepared

with povidone-iodine surgical scrub. Using sterile technique, the cisterna magna was punctured with a short (5 cm) 18-gauge spinal needle (with stylet). When clear CSF began to flow in pressure waves from the hub, 750 μCi of $^{99\text{m}}\text{Tc}$ labeled human serum albumin (in a volume of 0.2 ml or less) were injected. Because of the small volume of injected material, a small amount of cerebrospinal fluid was aspirated into the tuberculin syringe containing the radiopharmaceutical or the syringe was manipulated so that a small air bubble remained in it after injection. This was used to flush the last isotope from the lumen of the needle into the cistern.

Correct placement of the radiopharmaceutical was verified by recording transmitted pulsation waves from the needle, by the appearance of the clear CSF and by immediate scanning of the animal after injection. The radionuclide images were obtained using an Anger scintillation HP camera* with a high resolution collimator in both the vertex and lateral views. The vertex view was obtained by placing the animal prone with chin extended forward on the table and the lateral view with the animal lying on either side with the sagittal plane parallel to the table top. Images were obtained at 10 minutes, 2 and 4 hours after radiopharmaceutical injection.

Preparation of latex casts. A room temperature curing pigmented latex material (Microfil)† was employed to cast portions of the CSF space of normal rhesus monkeys. The brilliant yellow colored Microfil is ideal for visualization of the casts in the gross brain. The animal was anesthetized with pentobarbital and outlet ports were placed in one or both lateral ventricles stereotaxically. A cisternal tap was then made with an

* Nuclear-Chicago Corporation, Des Plaines, Illinois

† Canton Bio-Medical Products, Boulder, Colorado

18-gauge needle. Correct placements were verified by introducing a few drops of Evans blue tracer dye at the ventricular ports and observing its exit from the cisternal needle. Material for casts was mixed in the proportions: MV-122 yellow (4 ml); MV diluent (5 ml); MV curing agent (0.15 ml), to a total volume of 18 to 20 ml. The animal was sacrificed with an overdose of pentobarbital, and the mixture was introduced slowly through the cisternal needle until it appeared at the ventricular outlets. The animal was allowed to remain undisturbed until the latex material became solid (in situ overnight at 4°C). Necropsy was then performed by dissecting down to the casts, photographing them in situ and removing them intact for subsequent correlation.

III. RESULTS

Lateral and vertex scans of a normal Macaca mulatta at 10 minutes, 2 hours, and 4 hours after injection of radiopharmaceutical are shown in Figures 1 and 2. In the 25 normal animals investigated, there appeared to be a range of CSF flow rates reflected by radiopharmaceutical movement. Figure 1 shows the most typical pattern observed in these animals. Ten to thirty minutes following the radiopharmaceutical injection, filling of the cisterna magna and basal cisterns up to the cisterna ambiens is observed. By 2 hours, radioactivity is imaged over the lateral and posterior convexities of the cerebral cortex. By 4 hours the radiopharmaceutical is well distributed over the cerebral convexities. In normal primates, no ventricular entry of radiopharmaceutical was observed. A fairly common observation (approximately 20 percent) was slower flow, as illustrated in Figure 2, where movement of radiopharmaceutical above the tentorium is just beginning by the 4-hour image.

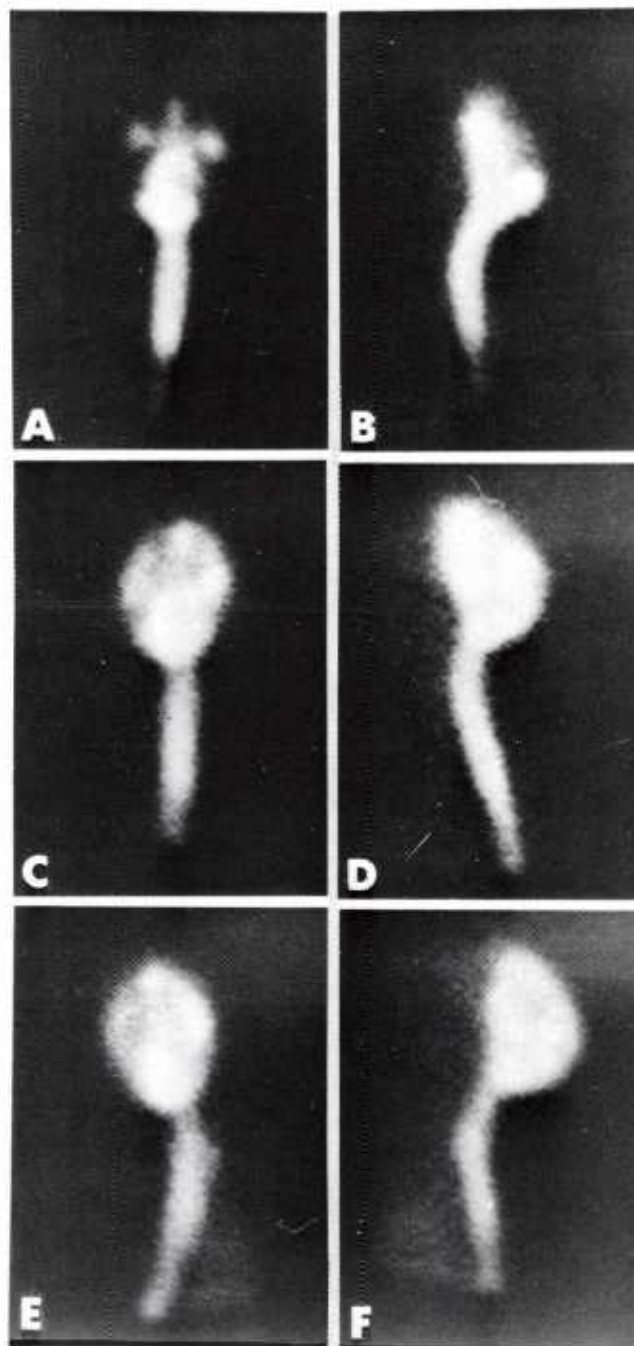


Figure 1. Normal cisternograms of the rhesus monkey after subarachnoid injection of 750 μCi $^{99\text{m}}\text{Tc}$ human serum albumin

- | | |
|-------------------|-------------------------|
| A. Vertex, 10 min | B. Left lateral, 10 min |
| C. Vertex, 2 h | D. Left lateral, 2 h |
| E. Vertex, 4 h | F. Left lateral, 4 h |

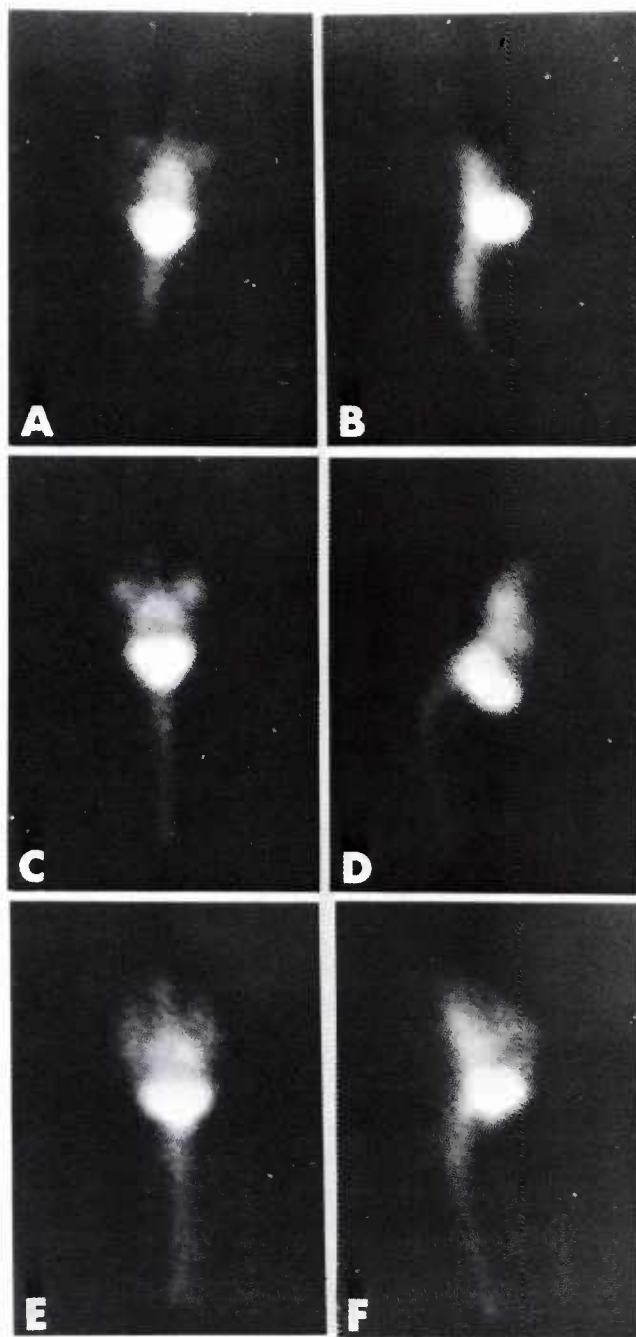


Figure 2. Slow normal cisternograms of the rhesus monkey after subarachnoid injection of 750 μCi $^{99\text{m}}\text{Tc}$ human serum albumin

A. Vertex, 10 min	B. Left lateral, 10 min
C. Vertex, 2 h	D. Left lateral, 2 h
E. Vertex, 4 h	F. Left lateral, 4 h

Anatomical localization of the spaces filled with radiopharmaceutical on cisternography was achieved with latex casts. Figure 3A is a photograph of such a latex preparation, in which the tentorium and all supratentorial structures have been removed and the specimen oriented in the vertex view (corresponding to that used during cisternography). When the projection drawing of this view and other views after removal of the cerebellum (Figure 3B) is compared with cisternographic images of the basal cisterns (Figure 3C), the ambient, interpeduncular, pontine, and great cisterns are readily identified, as well as regions of the cerebellopontine angle and pericallosal cisterns and of the cisterns of the sylvian fissures.

In contrast to the normal images presented above, Figure 4 illustrates the appearance of the enlarged ventricles of a primate with experimentally induced communicating hydrocephalus.³ Radioactivity is not observed over the cerebral convexities, but is localized to the ventricles and basal cisterns. The proximity of the lateral ventricles to the midline in this species is especially evident in the vertex view.

IV. DISCUSSION

The normal cisternographic series of the nonhuman primate Macaca mulatta appears to correlate well with the normal patterns described in humans. Comparison of abnormal images emphasizes the similarity to those reported in patients with communicating hydrocephalus. The anatomy of the basal cisterns is well demonstrated by the Microfil molds, and comparison with the radionuclide images adds to the validity of the clinical observations.

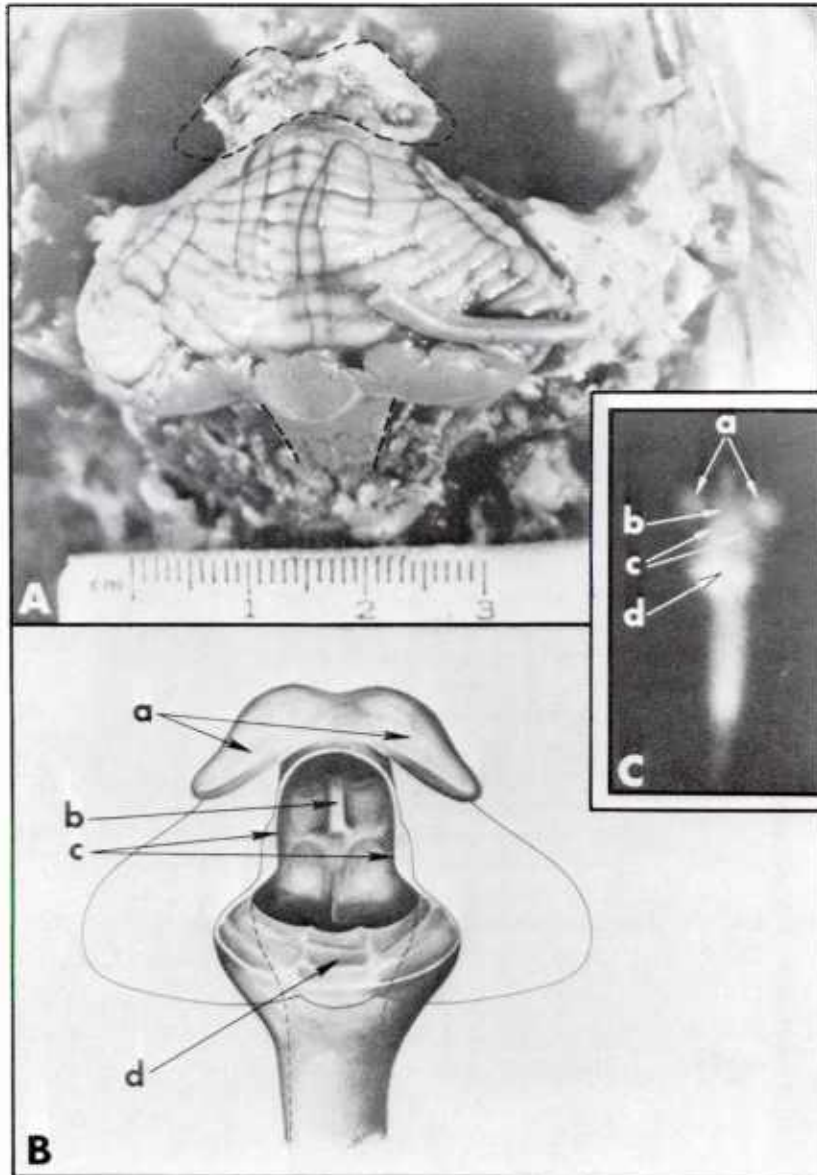


Figure 3. A. Vertex view of Microfil latex cast of basilar cisterns in situ. Tentorium and all supratentorial structures have been removed.
 B. Composite drawing from several latex casts, identifying the basilar cisterns. (a) Ambient cistern and cisterns of the sylvian fissures; (b) interpeduncular cistern; (c) pontine and cerebellopontine angle cisterns; and (d) great cistern.
 C. Normal vertex cisternogram 10 minutes after injection of 750 μCi $^{99\text{m}}\text{Tc}$ human serum albumin, outlining the basilar cisterns, labeled as in Figure 3B. The shadow between the regions labeled a represents radiopharmaceutical entering the pericallosal cistern.

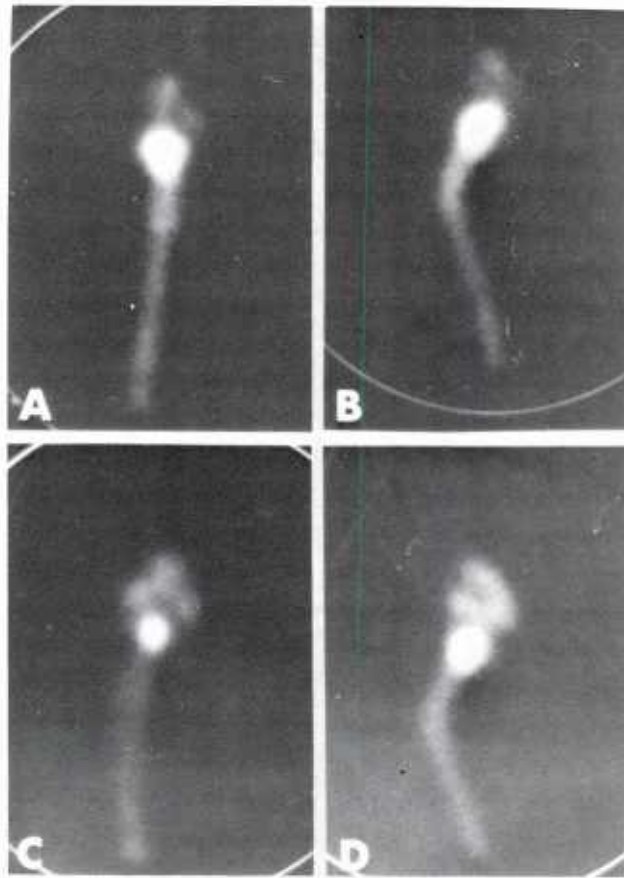


Figure 4. Cisternograms of primate with communicating hydrocephalus 40 days after implantation of Silastic in the anterior basilar cisterns. The entry of radiopharmaceutical ($750 \mu\text{Ci } ^{99\text{m}}\text{Tc}$ human serum albumin) into the lateral ventricles is characteristic of communicating hydrocephalus.

Proper intracisternal placement of isotope resulted in immediate well-defined imaging of the cisterna magna, basal cisterns, and a small region of subarachnoid space around the proximal cervical cord. The pattern of slower flow presented in Figure 2 apparently represents a normal variant of CSF dynamics in these animals. It is not that produced by an improper subdural placement of labeled albumin, which results in a bolus of radioactivity localized near the cisterna magna that moves almost imperceptibly with time.

In observing the development of communicating hydrocephalus by cisternography correlated with necropsy studies, it is apparent that minimal to moderate ventricular dilatation can occur before radiopharmaceutical entry is evident on the images. Rendering the injected casting material radioactive before instillation or subsequent activation of the casts in situ within the ventricles is anticipated for quantitative studies of the degree of ventricular dilatation or radiopharmaceutical entry necessary to resolve the ventricles by cisternography.

The nonhuman primate provides a central nervous system most closely related to man anatomically and physiologically. Radioisotope cisternography provides an atraumatic, reproducible means for visualizing the CSF flow in the primate. The similarity between cisternographic patterns observed in these animals and in patients with communicating hydrocephalus strengthens the validity of the nonhuman primate model for further study of this disease.

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13. ABSTRACT

Normal imaging of cerebrospinal fluid (CSF) flow in the primate Macaca mulatta using ^{99m}Tc labeled human serum albumin shows flow from the basal cisterns over the cerebral cortex in 4 hours. Anatomical correlation of basal cisterns with cisternographic images was demonstrated with latex casts of the normal CSF spaces. Cisternographic images from nonhuman primates with experimental communicating hydrocephalus have entry of radiopharmaceutical into the lateral ventricles and are presented for comparison. Cisternography is a useful technique for evaluating such primate disease models, since normal and pathologic images parallel those obtained in man.